Reviewer’s report

Title: Adolescent Polycystic Ovary Syndrome according to the International Evidence-Based Guideline

Version: 2 Date: 14 Dec 2019

Reviewer: Corrine Welt

Reviewer's report:

The authors have discussed their reasoning. There are still some small changes needed for the PCO Morphology section.

Please note that the fact that I cannot agree with the recommendation relates to the issue that the arguments in the section, the references provided and the available data do not support the comment that ultrasound should not be used for up to 8 years after menarche as a criteria for PCOS. The 8 year post menarche cutoff remains poorly justified. At minimum, the paragraph needs more detail as the references are not supportive of 8 years. 8 years does not have any bearing to age 20 years as the age at which ovaries are largest, the 2-4 years of expected irregular menses post menarche or the age of the HPG axis maturation. It appears to be tied most strongly to, as yet, unpublished data. Therefore, the guidelines should include the data or wait for the publication so that readers can understand the reasoning. If these data are part of the technical information, the technical information should be provided as the link is not working.

The rebuttal also raises issues around overlap with adult guidelines. "Of these, there were only 3 studies in females younger than 18 years that have been reported in the original manuscript. The remaining studies in women older than 18 years (n=12) are included in the technical report of the guidelines (which we referred to in the manuscript) and listed below. These were not included in the manuscript as the manuscript focus was adolescents." Are you saying that women older than 18 years are not adolescents? Therefore, when your guidelines cross age 18 and reach into the adult guidelines, I believe you need to note that these guidelines will conflict with adult guidelines.

The sentence in the second paragraph, " Furthermore, the correlation between ovarian morphology (ovarian size and follicle numbers) and menstrual function is inconsistent in adolescence and early adulthood. [55]" does not recognize that the manuscript used older criteria for PCOM and that even then, 40% of the subjects met polycystic ovary syndrome criteria based on irregular menses and hyperandrogenism. Therefore, the sentence is misleading, as is the response to the comment. Please revise.

In other words, when stating that, "In evaluating the evidence indeed multi-follicular ovaries do persist 5 to 8 years post menarche as previously reported in the manuscript (Reference 55 - Kristensen SL, Ramlau-Hansen CH, Ernst E, Olsen SF, Bonde JP, Vested A, Toft G: A very large proportion of young Danish women have polycystic ovaries: is a revision of the Rotterdam criteria needed? Human reproduction (Oxford, England) 2010, 25(12):31173122)." the comment does not take into consideration that this is not a study of multifollicular ovaries and is not longitudinal. As above, the manuscript used older criteria for PCOM and even then, 40% of the subjects met polycystic ovary syndrome criteria based on irregular menses and hyperandrogenism. Therefore, it is not supportive of the concept that multifollicular ovaries persist post menarche.
Importantly, please consider this rebuttal. "Additionally, we have data on longitudinal changes from childhood through to early adulthood. (Follow up data of the Australian RAINE study [a large prospective cohort from pregnancy] - manuscript under review). Very importantly where polycystic ovarian morphology (PCOM) was included in the diagnostic criteria in women <8 years post menarche, the diagnosis rate of PCOS was 30%. Where PCOM was not included, the diagnosis rate in adolescence was 15%, akin to the adult rate. Most importantly only those diagnosed not using PCOM <8 years went on to have clear longer term PCOS. The implications of using PCOM in women less than 8 years post-menarche are considerable as there will be a high rate of over diagnosis of PCOS, which the guidelines are aiming to reduce." These as yet unpublished data sound as if they influenced the 8 year mark extensively. Therefore, it is very difficult for the reader to have any concept of the longitudinal ovarian morphology results without those data available.

The technical report is not accessible from the link. If the technical report is critical for understanding, please send it for review.

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If not, please specify what is required in your comments to the authors.

Yes

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